Abstracts

1. FUNDAMENTAL STUDIES IN CHEMOTHERAPY OF TUBERCULOSIS

Part 55. Studies on the Influence of Antituberculous Agents upon the Function of Pseudoeosinophilic Leucocytes and Blood Picture of Experimental Animals No. 1. Observation in Healthy Rabbits

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A series of experiments was planned in an attempt to investigate the influence of antituberculous agents upon the migration velocity of pseudoeosinophilic leucocytes of experimental animals and upon the phagoytic power of those leucocytes against carbon particles. The present paper describes the results of the study concerning the influence of one single administration of one of the five agents, o-aminophenol(OM), streptomycin(SM), p-aminosalicylic acid(PAS), p-acetylaminobenzaldehyde thiosemicarbazone(TBI) and isonicotinic acid hydrazide (INAH) upon the two functions of the pseudoeosinophilic leucocytes of healthy rabbits.

The data obtained may be summarized as follows :

1) Both functions were promoted temporarily after the administration of an adequate dose of each drug, and suppressed temporarily after the administration of an excessive dose. But when the dose is midway between the two, suppression of phagocytic power and increase of migration velocity were observed.

2) When the drugs are given to rabbits in the same ratio as when they are therapeutically administered to humans the promoting effect of these drugs on the functions of the rabbit leucocytes was found to be as follows;

$$PAS \geqq INAH > OM \fallingdotseq SM \fallingdotseq TBI.$$

2. FUNDAMENTAL STUDIES IN CHEMOTHERAPY OF TUBERCULOSIS

Part 55. Studies on the Influence of Antituberculous Agents upon the Function of Pseudoeosinophilic Leucocytes and Blood Picture of Experimental Animals No. 2. Observation in Experimental Tuberculous Rabbits (I)

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In a previous paper, the data from a series of experiments were reported concerning the influence of one single administration of antituberculous agents upon the migration velocity of the pseudoeosinophilic leucocytes of healthy rabbits and upon the phagocytic power of these leucocytes against carbon particles. The present paper describes the results of the study concerning the influence of successive

administration of daily doses of either 250 mg OM or 500 mg PAS upon the two functions of the leucocytes. The drug was administered in single daily doses.

Experiment I.

The following three groups of rabbits were used as the subject:

Groups I and II : Rabbits which had received one single intravenous injection of either 1.0 mg (group I) or 5.0 mg(group II) of a living culture of a strain of human-type tubercle bacilli "H37Rv"

Group III : Healthy rabbits

Each group was divided into three subgroups; the first subgroup was treated with OM, the second with PAS and the third was left alone as the control.

The treatment began 4 weeks after infection and the examination of the leucocyte functions was carried out once every seven days during the period of treatment.

The results obtained are as follows:

1) Between groups I and II, and among their subgroups, no definite difference in the temporary promotion of the leucocyte functions was observed after the administration of the drug.
2) The leucocyte functions of the treated rabbits of group II differed strikingly from those of all other rabbits, the temporary promotion of the leucocyte functions being far less in group II than in the others.
3) No lasting change of the leucocyte functions was observed as a result of the successive treatment with the above-mentioned dose of either OM or PAS.

Experiment II.

Rabbits which had received one single intravenous injection of 5.0 mg of a living culture of human-type tubercle bacilli "H37Rv" were divided into three groups, and treated as follows:

Group I. Rabbits treated with OM
Group II. Rabbits treated with PAS
Group III. Untreated rabbits as control

The treatment began 5 days after infection and the examination was carried out once every 5 days during the period of treatment. The results obtained were as follows:

The degree of lasting suppression of the two functions of the leucocyte of the rabbits was almost identical in all the three groups, that is to say, the change of the leucocyte functions was not influenced by the administration of the above-mentioned dose of either OM or PAS.

3. FUNDAMENTAL STUDIES IN CHEMOTHERAPY OF TUBERCULOSIS

Part 55. Studies on the Influence of Antituberculous Agents upon the Function of Pseudoeosinophilic Leucocytes and the Blood Picture of Experimental Animals

No. 2. Observation in Experimental Tuberculous Rabbits (II)

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A) A series of experiments was carried out to study the influence of one single administration of either 250 mg OM or 500 mg PAS upon the hemogram of rabbits.

The following three groups of rabbits were used as the subject:

Groups I and II: Rabbits which had received one single intravenous injection of either 1.0 mg

(group I) or 5.0 mg(group II) of a living culture of a strain of human-type tubercle bacilli "H37Rv"

Group III: Healthy rabbits

Each group was divided into three subgroups; the first subgroup was treated with OM, the second with PAS and the third was left alone as control.

The treatment began 4 weeks after infection and the examination of the hemogram was carried out once every seven days during the period of the treatment.

The results obtained were as follows:

1) No variation of the erythrocyte count or of the hemoglobin content was observed in any of the groups after the administration.
2) No appreciable change of the leucocyte count was observed except in a few cases of groups I and III which showed slight decrease of the count shortly after the administration and then temporary slight increase.
3) After the administration temporary increase of pseudoeosinophilic leucocyte count was observed in all the groups, and the degree of the increase was in the following order.

group III> group I> group II

4) Decrease of lymphocyte count was observed in all the groups.
5) Monocytes, and eosinophilic and basophilic leucocytes showed no tendency to increase or decrease.
6) The mean number of nuclei of pseudoeosinophilic leucocytes remained the same or showed a slight decrease.

B) Additional experiments were carried out, in the same way as Experiment A, to study the influence of successive administration of either 250 mg OM or 500 mg PAS upon the hemogram of rabbits, but no lasting change of the hemogram was observed to occur.

Summary of Experimental Data of No. 1 to No. 2

The influence of OM, SM, PAS, TBI and INAH administered separately upon the migration velocity of pseudoeosinophilic leucocytes and their phagocytic power against carbon particles in healthy rabbits and that of OM and PAS upon the two functions and the hemogram in experimental tuberculous rabbits were investigated.

The results described previously may be summarized as follows:

I) The changes of the functions of pseudoeosinophilic leucocytes after one single administration of the above-mentioned drugs

In healthy rabbits: Both functions are promoted temporarily after the administration of either OM (60–250 mg) or SM (60–250 mg) or PAS (125–500 mg) or TBI (5–15 mg) or INAH (5–15 mg).

In experimental tuberculous rabbits: In rabbits infected with 1.0 mg "H37Rv" both functions were promoted temporarily after one single administration of either 250 mg of OM or 100 mg of PAS as in healthy rabbits, and in rabbits infected with 5.0 mg "H37Rv", the promotion of the functions was far less than in the former.

II) The changes of the hemogram after one single administration of above-mentioned dose of either OM or PAS in healthy and experimental tuberculous rabbits

The pseudoeosinophilic leucocyte count increased and the lymphocyte count decreased temporarily after the administration. The degree of increase of the cells was in the following order:

Healthy rabbits>Rabbits infected with 1.0 mg "H37Rv">Rabbits infected with 5.0 "H 37 Rv"

III) The change of successive treatment with the above-mentioned dose of either OM or PAS upon the functions of leucocytes and the hemogram in experimental tuberculous rabbits

No lasting change of the functions or the hemogram was observed as a result of the treatment.

4. FUNDAMENTAL STUDIES IN CHEMOTHERAPY OF TUBERCULOSIS

Part 56. Experiments on the Antituberculous Effectiveness of o-Aminophenol, p-Aminosalicylic Acid and Dihydrostreptomycin against Dihydrostreptomycin-resistant Strains of *Mycobacterium tuberculosis*

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Received for publication, July 5, 1955

Evidence has been presented to show that o-aminophenol is as effective against Dihydrostreptomycin-resistant strains of *Myco. tuberculosis* as against the sensitive strain.

5. FUNDAMENTAL STUDIES IN CHEMOTHERAPY OF TUBERCULOSIS

Part 57. Study on the Influence of Anti-tuberculous Agents upon Digestive Enzymes.

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The present study is concerned with gastrointestinal toxicity of anti-tuberculous agents with special reference to their influence upon various digestive enzymes.

The anti-tuberculous agents studied were streptomycin, isonicotinic acid hydrazide, p-aminosalicylic acid, 4-acetylaminobenzaldehyde thiosemicarbazone (Tibione) and o-aminophenol. The digestive enzymes used were proteases, including pepsin and trypsin, α-amylase and lipase. Peptic digestion of edestin was estimated by the method of Fuld and Levison. Trypsin was assayed by the Fuld and Gross' procedure, using casein as a substrate. The estimation of α-amylase activity was carried out by the Wohlgemuth's method. The tributyrin-hydrolyzing activity of lipase was determined by titration with 0.1 N KOH of the liberated butyric acid. The anti-tuberculous agents to be tested were previously added to the substrate solution, and the degree of enzymatic hydrolysis of the substrate was compared with that obtained in the absence of the agent.

The results obtained are summed up as follows : All the anti-tuberculous agents tested showed no significant effect upon the digestive enzymes, except that p-aminosalicylic acid, in dilutions of 1:200—400, exhibited a definitely inhibitory effect on peptic digestion of edestin.

6. STUDIES ON THE FUNCTION OF LEUCOCYTES IN PULMONARY TUBERCULOSIS PATIENTS TREATED WITH ISONICOTINIC ACID HYDRAZIDE

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The change of the migration velocity of neutrophilic leucocytes and of their phagocytic power against carbon particles were studied in pulmonary tuberculosis patients after one single administration of 0.2 to 0.4 gm INAH.

It was found that both functions were impaired for 7—10 hours or longer and was lowest at 1 hour after the administration. Then some experiments were carried out to study the influence of continuous administration of daily doses of 0.2 to 0.4 gm INAH upon the migration velocity of the leucocyte. In these experiments, promotion of the migration velocity of neutrophilic leucocytes appeared within a few weeks accompanied by improvement of clinical findings and persisted throughout the period of treatment(2.5—6 months).

7. STUDIES ON THE INFLUENCE OF THORACIC SURGICAL OPERATION UPON THE FUNCTION OF LEUCOCYTES IN PULMONARY TUBERCULOSIS PATIENTS

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The influence of thoracoplasty, replasty, cavernostomy and cavernectomy upon the functions of neutrophilic leucocytes in pulmonary tuberculosis patients was studied. The results obtained were as follows:

1) The migration velocity decreased, the minimum value being reached and the normal value regained, 2 to 4 days and 9 to 17 days respectively after operation.
2) The phagocytic power also decreased, being lowest and recovering completely, 1 to 3 days and 8 to 19 days respectively after operation.
3) The suppression of phagocytic power was found to be more marked than the decrease of migration velocity.
4) The larger the extent of operation was, the longer was the period after operation needed for the recovery of the impaired functions.
5) The mean number of nuclei of neutrophilic leucocytes showed Sugiyama's "degenerative left shift" and recovered concurrently with restoration of blood picture.
6) The leucocyte functions recovered more quickly than erythrocyte sedimentation rate.

8. FORMATION OF TUBERCULIN BY WASHED TUBERCLE BACILLI IN CITRATE SOLUTION

Part 5. On the Production of Citrate-tuberculin by an Isonicotinic-acid-hydrazide-resistant Variant of Tubercle Bacilli

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Received for publication, Sept. 23, 1955

An INAH-resistant variant of *Myco. tuberculosis* derived from human tubercle bacilli, Aoyama B, by serial transfers in Kirchner's medium containing isonicotinic acid hydrazide(INAH), was tested for the production of tuberculin by the method of incubating the washed bacilli in a citrate solution. It was demonstrated that the INAH-resistant strain of tubercle bacilli yielded citrate-tuberculin nearly as potent as that produced by the parent INAH-sensitive strain.

9. ON HUMAN BEINGS WHOSE TUBERCULIN REACTION REMAINS NEGATIVE AFTER REPEATED BCG INOCULATION

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A series of experiments was carried out regarding the disposition of the human beings whose tuberculin reaction remained negative after repeated BCG inoculation.

Sixty such subjects(group A) and 17 control subjects whose tuberculin reaction became positive after only one BCG inoculation(group B) were involved in these experimets. The items studied included tuberculin test, blood typing, number of leucocytes, leucogram, Widal reaction after typhoid vaccine injection, slide cell culture and phagocytosis of leucocytes against *Myco. tuberculosis* and BCG.

The results obtained were as follows:

I) The people who showed negative results in old tuberculin(1/2,000, 0.1ml) skin tests given after repeated BCG inoculation were found to show positive results when tested with 2.5γ/0.1 ml of o-Aminophenol Azo-Tuberculin "BCG".

2) No close relation was observed between tuberculin reaction and blood typing, i. e., our observation disproved the hypothesis that only people of B blood type are apt to fail to undergo Mantoux conversion after repeated BCG inoculation.

3) The phagocytic power of leucocytes against BCG and the growth inhibitory power of the blood against *Myco. tuberculosis* and BCG were greater in group A than in group B.
4) In the experiments, in which groups A and B received intracutaneous injection of typhoid vaccine, the results of the Widal test performed thereafter once every ten days did not run parallel to tuberculin reactivity.

10. SKIN TEST WITH O-AMINOPHENOL AZO-TUBERCULIN "BCG" IN HUMAN BEINGS WHOSE SKIN REACTION TO OLD TUBERCULIN REMAINS NEGATIVE IN SPITE OF REPEATED BCG INOCULATION

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It has already been noticed that there are some people in whom tuberculin skin tests persistently show negative results in spite of repeated BCG inoculation.

This paper describes several cases in which people, showing negative results when tested with 0.05 "mg" of old tuberculin(OT) after repeated BCG inoculation, were all found to react positively to 0.001 mg of o-Aminophenol Azo-Tuberculin "BCG" (OA-Azo-T"BCG"). In addition, naturally infected people were found to react positively to the same degree to the above-mentioned doses of OA-Azo-T"BCG" and OT and to 0.000,05 mg of OA-Azo-T"Human", while BCG inoculated people free from natural infection have a lower sensitivity to 0.000,05 mg of OA-AzO-T"Human" than to 0.05 "mg" of OT.

Thus it is suggested that skin test with OA-AzO-T "BCG" is effective for the detection of weak tuberculin allergy after BCG inoculation, and also that simultaneous skin test with the above-mentioned doses of OA-Azo-T"BCG" and OA-Azo-T "Human" might profitably be used for the differential diagnosis of BCG inoculation and natural infection.

11. STUDIES ON THE METABOLISM OF *MYCOBACTERIUM TUBERCULOSIS*

PART 2. INFLUENCE OF THE CONSTITUENTS OF CULTURE MEDIUM OF *Mycobacterium tuberculosis*

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The influence of adding various substances to the culture medium on the respiration of various strain of tubercle bacilli, *Myco. phlei* and BOK (a mutant strain of a human type of tubercle bacilli) was thoroughly investigated, the oxygen consumption being measured by Warburg's apparatus.

The results of the experiments are shown in the table 1.

Table 1. Influences of various substances on the respiration of *Mycobacterium tuberculosis* suspended in phosphate-buffered solution, pH 7.0

Substances tested	Range of substance concentrations in medium	Strains of Mycobacteria employed	Result	
			Reading after	Increased(+), decreased(−) or unchanged(0) oxygen uptake was observed in concentration (s)
Glycerol	0.5M/1 ↑ ↓ 0.000,01M/1	Human type $H_{37}Rv$, Aoyama, H_2	4 hours	+, +, + } 2.5~0.1M/1
		Bovine type 10		+ 2.5~0.001M/1
		Avian type A_{67}, Takeo		+ 2.5~0.01M/1
		Others M. phlei, BOK		+ 2.5~0.000,01M/1
Sodium glutamate	0.1M/1 ↑ ↓ 0.000,01M/1	Avian type A_{67}, Takeo	6 hours	0 for A_{67} + 0.1~0.001M/1 for Takeo
Asparagin				0 for both
Sodium citrate			4 hours	− 0.1M/1
Magnesium sulphate	0.005M/1 ↑ ↓ 0.001M/1			0 for both
Ferr. ammon. cit.	0.5% ↑ ↓ 0.000,5%			+ 0.5~0.005%
Inactivated human serum	20% ↑ ↓ 5%	Human type $H_{37}Rv$	6 hours	+ 20%
		Avian type Takeo		+ 20~5%
Polytamin (Amino acids preparation)	30% ↑ ↓ 5%	Human type $H_{37}Rv$, Aoyama, H_2	4 hours	+, +, + } 30~20%
		Bovine type 10		+ 30%
		BCG		+ 30~20%
		Avian type A_{67}, Takeo		+ 30~10%
		Others M. phlei, BOK		+, + } 30~5%
				+ 30%

12. STUDIES ON THE METABOLISM OF *MYCOBACTERIUM TUBERCULOSIS*

PART 3. INFLUENCE OF ANTITUBERCULOUS AGENTS UPON THE RESPONSE OF TUBERCLE BACILLI TO GLYCEROL AND POLYTAMIN

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It has been previously shown that both glycerol and polytamin considerably promote the respiratory metabolism of *Myco. tuberculosis*. The present study was directed to the determination of the effect of certain antituberculous agents upon the response of *Myco. tuberculosis*, *Myco. phlei* and BOK (a mutant strain of a human type tubercle bacillus) to glycerol and polytamin.

The followings are the results obtained:

In very low concentrations(SM 1:800, INAH 1 : 100,000, PAS 1:800 and OM 1 : 800,000) the agents did not affect the response of any of the organisms tested to either glycerol or polytamin, but in higher concentrations the agents were found to affect the response of both human type tubercle bacillus "H_2" strain and avian type tubercle bacillus "Takeo" strain to a considerable extent. The effect of the highest concentrations of the agents used shown in the table 1.

Table 1. Influence of antituberculous agents upon the response of tubercle bacilli to glycerol and polytamin

Species	Strain	SM 1: 100		LNAH 1:200		PAS 1:100		OM 1:800	
		G	P	G	P	G	P	G	P
M. tuberculosis var. *hominis*	$H_{37}Rv$	0	—	—	(—)	0	0	+	+
	Aoyama	0	—	(—)	(—)	+	0	+	+
	H_2	∓	0	—	—	+	±	+	+
M. tuberculosis bovis	10	—	0	—	(—)	+	±	+	+
BCG		0	—	0	∓	∓	—	+	0
M. tuberculosis avium	A_{67}	∓	∓	∓	—	0	—	0	+
	Takeo	—	—	—	0	—	—	—	—
M. phlei		∓	0	—	—	+	0	0	0
BOK		—	0	0	±	—	0	—	(—)

G : response of Mycobacterium to glycerol
P : response of Mycobacterium to polytamin
+ : excessively accelerated
± : slightly accelerated
0 : unchanged
∓ : slightly inhibited
— : inhibited
(—): with inhibition of endogenous rate

13. STUDIES ON THE METABOLISM OF *MYCOBACTERIUM TUBERCULOSIS*

PART 4. EFFECT OF VARIATION OF pH ON THE RESPONSE OF *Mycobacterium tuberculosis* TO GLYCEROL

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The relation between pH and the response of human type tubercle bacillus "H37Rv" and avian type tubercle bacillus "Takeo"strain to glycerol was investigated.

The results of the experiments were as follows:

1) In glycerol respiration of "H 37 Rv" strain and BCG, the highest oxygen uptake was observed at pH 7.5 and the value decreased toward the side of acidity of the medium.
2) In glycerol respiration of "Takeo" strain, the greater oxygen uptake was observed on the side of acidity of the medium.

14. STUDIES ON THE RESISTANCE OF MICROORGANISMS TO VARIOUS CHEMICALS

PART 3. ON THE EFFECT OF SIMULTANEOUS EXPOSURE TO TWO CHEMICALS

No. 1. OBSERVATION ON *Myco. tuberculosis* IN VITRO

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A) Using Kirchner's media containing streptomycin(SM) plus other agents such as p-aminosalicylic acid(PAS), Tibione(TBI), o-aminophenol(OM), isonicotinic acid hydrazide(INAH), p-aminobenzoic acid (PABA), methionine and sulzol individually, change of the tuberculostatic power of SM against human tubercle bacilli "H_2" strain was examined by means of culture *in vitro*. Similar experiments were carried out concerning PAS and TBI individually in place of SM.

The results of the experiments were as follows:

1) For enhancing the tuberculostatic power of SM, SM+PAS and SM+INAH were found to be most effective, followed by SM+OM and SM+sulzol.
2) For enhancing the power of PAS, PAS+OM was found to be most effective, followed by PAS+TBI.
3) For enhancing the power of TBI, TBI+INAH was found effective.

B) By the same experimental method as A, change of the tuberculostatic power of SM against SM-resistant "H_2" strain was examined, and it was found that SM+INAH, SM+PAS and SM+OM were excessively effective for the enhancement of the tuberculostatic power of SM.

C) By the same experimental method as A, change of the tuberculostatic power of PAS against PAS-resistant "H_2" strain was examined, and it was found that PAS+INAH and PAS+OM were most effective for enhancing the tuberculostatic power of PAS, followed by PAS+SM and PAS+TBI.

15. STUDIES ON THE RESISTANCE OF MICROORGANISMS TO VARIOUS CHEMICALS

Part 3. On the Effect of Simultaneous Exposure to Two Chemicals

No. 2. Observation on *Myco. tuberculosis* in vitro by Successive Culture

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A) Using Kirchner's media containing streptomycin (SM) plus other agents such as p-aminosalicylic acid(PAS), Tibione(TBI), o-aminophenol(OM), isonicotinic acid hydrazide(INAH), p-aminobenzoic acid (PABA), methionine and sulzol individually, development of SM-resistant human tubercle bacilli "H_2" strain and change of the tuberculostatic power of SM against"H_2" were examined by means of successive culture. The same experiments were carried out concerning PAS and TBI individually in place of SM. The results of the experiments were as follows:

1) SM+OM and SM+PAS showed the strongest effect for retarding the appearance of SM-resistant bacilli and for enhancing the tuberculostatic power of SM, and were followed by SM+INAH.
2) PAS+OM, PAS+TBI and PAS+INAH were somewhat effective for enhancing the tuberculostatic power of PAS, and only slightly effective for retarding the development of PAS-resistance of the bacilli.
3) TBI+OM and TBI+INAH were effective for enhancing the tuberculostatic power of TBI. Appearance of TBI-resistant bacilli was not noticed within the period of this experiments, nor when TBI was used alone.

B) Using the same experimental method, change of tuberculostatic power of SM against SM-resistant "H_2" strain and development of drug-resistance of the bacilli were examined. The results of the experiments were as follows:

Exposure to SM+PAS and SM+INAH resulted in the development, respectively, of PAS-resistance and INAH-resistance of the bacilli. Addition of OM, PAS and INAH, individually, to SM produced enhancement of the tuberculostatic power of SM at the earlier stages of the successive culture but the opposite effect in the later stages.

C) Using the same experimental method, change of tuberculostatic power of PAS against PAS-resistant "H_2" strain and change of drug-resistance of the bacilli were examined. The results of the experiments were as follows:

In this case also restoration of PAS-sensitivity of the bacilli did not occur. INAH-resistance developed in spite of the exposure to PAS+INAH, whereas PAS+SM, PAS+OM and PAS+INAH were found effective for enhancing the tuberculostatic power of PAS and followed by PAS+TBI.

16. STUDIES ON THE RETICULO-ENDOTHELIAL SYSTEM IN TUBERCULOSIS

Part 1. Effect of Antituberculous Agents on the Reticulo-endothelial Function, Especially on the Congo-red Index

No. 1. Experiments on Healthy Rabbits

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By means of Adler-Remann's congo-red method, a series of experiments was carried out to study the influence of various antituberculous agents such as o-aminophenol(OM), p-aminosalicylic acid(PAS), isonicotinic acid hydrazide(INAH), Tibione(TBI) and streptomycin(SM) upon the function of the reticulo-endothelial system of normal rabbits. The results obtained were as follows:

1) Promotion of the function of the reticulo-endothelial system of rabbits was observed when an adequate dose of each drug(OM) 0.3 gm, PAS 2.0 gm, SM 0.1 gm, INAH 10 mg and TBI 10 mg per kilogram of body weight) was administered individually by subcutaneous route. But suppression was observed when a larger dose of each drug (OM 0.5 gm, PAS 4.0 gm, SM 0.4 gm, INAH 40 mg and TBI 30 mg per kilogram of body weight) was administered in the same way as mentioned above.
2) When the adequate doses of OM and another agent were administered together the function suffered suppression, but when the doses were reduced the function was promoted by the simultaneous administration of the two agents.

17. STUDIES ON THE RETICULO-ENDOTHELIAL SYSTEM IN TUBERCULOSIS

Part 1. Effect of Antituberculous Agents on the Reticulo-endothelial Function, Especially on the Congo-red Index

No. 2. Experiments on Healthy Adult Human Beings

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By means of Adler-Reimann's congo-red method, some experiments were carried out to study the influence of various antituberculous agents such as o-aminophenol (OM), p-aminosalicylic acid(PAS), isonicotinic acid hydrazide(INAH), Tibione(TBI) and streptomycin(SM) upon the function of the reticulo-endothelial system of healthy humans.

The results obtained were as follows:

1) No appreciable change of the function of the reticulo-endothelial system was noticed when 0.5 or 1.0 gm of OM, 5.0 or 7.0 gm of PAS, 0.1, 0.3 or 0.5 gm of INAH and 0.05 or 0.1 gm of TBI was given orally and 1.0 gm of SM intramuscularly separately.
2) Slight promotion was observed after the administration of 1.5 gm OM and 2.0 gm SM individually.

18. STUDIES ON THE RETICULO-ENDOTHELIAL SYSTEM IN TUBERCULOSIS

Part 2. Effect of Old Tuberculin and o-Aminophenol Azo-Tuberculin "Human" on the Reticulo-endothelial Function

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By means of Adler-Reimann's congo-red method, a series of experiments was carried out to study the influence of old tuberculin(OT) and o-Aminophenol Azo-Tuberculin"Human" (OA-Azo-T"Human") upon the function of the reticulo-endothelial system of normal and tuberculous rabbits. The results obtained were as follows:

1) Promotion of the function of the reticulo-endothelial system of normal rabbits was observed when 10 "mg" of OT was injected subcutaneously. But no effect was observed when 0.01 mg of OA-Azo-T"Human" was injected subcutaneously.
2) Promotion of the function of the reticulo-endothelial system of tuberculous rabbits was observed when 10 "mg" of OT and 0.01 mg of OA-Azo-T"Human" were injected individually by subcutaneous route.
3) Increase of the leucocyte count was found in the blood picture of tuberculous rabbits 24 to 48 hours after injection of 10"mg" of OT. This increase was mainly due to the increase of pseudoeosinophilic leucocytes. Administration of 0.01 mg of OA-Azo-T"Human" to a tuberculous rabbit brought about no change in its blood picture.

19. CLINICAL STUDIES ON THE BRONCHI OF PULMONARY TUBERCULOSIS PATIENTS

Part 1. A Supplemental Study of the Tuberculous Bronchitis

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Bronchoscopic examination was carried out upon fifty adult tuberculosis patients in order to find the correlation between pulmonary tuberculosis and bronchial tuberculosis. The results obtained may be summarized as follows:

1) Bronchial lesions were observed more frequently in pulmonary tuberculosis of the form called "mixed" by roentgenologists as compared with either productive or exudative or cirrhotic form. Between the latter three forms of pulmonary tuberculosis no appreciable difference was noticed in the frequency of formation of bronchial lesions.
2) Severe bronchial tuberculosis occurred somewhat more frequently on the left side than on the right.
3) There was observed definite difference in the frequency of formation of bronchial lesions between the cases of pulmonary tuberculosis with and without cavity. To be exact, the number of patients

having bronchial tuberculosis was 35 among the 42 with cavity(or 83%) and 2 among the 8 without cavity(or 25%).

4) The quantity of bacilli in the sputum was the most significant of all the factors that cause bronchial tuberculosis.

20. CLINICAL STUDIES ON THE BRONCHI OF PULMONARY TUBERCULOSIS PATIENTS

Part 2. Bacteriological Study of the Secretions Drawn from the Bronchi

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A series of experiments was carried out in an attempt to investigate the relation between pulmonary tuberculosis and non-acid-fast bacilli in bronchial secretion drawn by Jackson's bronchoscopical method.

Bacteriological examination, microscopic and biological, of the bronchial secretion and the sputum was carried out sise by side. In this work, the following two groups of human beings were employed as the subject.

Group I. 27 pulmonary tuberculosis patients.

Group II. 2 acute bronchitis patients and 3 healthy persons as the control.

The results obtained may be summarized as follows:

1) In the bronchial secretion, non-acid-fast bacilli were observed in 8 of the 12 pulmonary tuberculosis patients examined. On the other hand, in the sputum these bacilli were observed in all of the 27 patients, and the kinds of bacilli found in bronchial secretion were all demonstrable in the sputum.
2) It was clearly noticed that the kinds of bacilli ran parallel with the degree of pulmonary and bronchial lesions.
3) In passing, tubercle bacilli in bronchial secretion of a patient treated with antituberculous agents occasionally showed different degrees of resistance against such agents according as they came from the right bronchus or the left.

21. INVESTIGATIONS OF PNEUMOTHORAX AND PNEUMOPERITONEUM IN PULMONARY TUBERCULOSIS

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In the present investigation, the following two groups of adult tuberculosis patients were employed

as the subject.

1) Group A : Twenty-seven patients for whom the use of artificial pneumothorax treatment was indisputably indicated.
2) Group B : Thirty patients selected at random for the use of pneumoperitoneum treatment.

Each patient received no other treatment except the kind indicated above for his group and the effectiveness of these treatments was compared.

The investigation, in which subjective complaints, body temperature, body weight, erythrocyte sedimentation, tubercle bacilli in sputum, x-ray finding and side effects were observed, revealed that:

1) Successful results were obtained more frequently in long-term treated cases than in short-term ones, but careful attention has to be paid to avoid atelectasis and other side effects.
2) The effectiveness of pneumothorax depends mainly on the absence of pleural adhesion. Therefore the condition of lung contraction has to be carefully observed. There are many cases in which the treatment has to be discontinued owing to the occurrence of pleural adhesion or of pyothorax.
3) On the contrary, pneumoperitoneum is widely applicable because it has few contra-indications and minimal complications.
4) Advisability of superseding pneumothorax and pneumoperitoneum with chemotherapy or surgical operation must be kept in mind not only because the former methods of treatment have certain limitations for efficacy but because pulmonary lesions treated by them frequently leave behind tuberculomas or filled-in cavities.

22. STUDIES ON THE INFLUENCE OF SERUM UPON THE HEMOLYSIS CAUSED BY STREPTOLYSIN S

I. On the Mode of Anti-streptolysin S Action of Serum
II. On the Thermo-stabilizing Effect of Serum upon Streptolysin S

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Data are presented which strongly suggest that the inhibition of the hemolytic effect of streptolysin S by normal serum is not due to the destruction of the toxin molecule or the irreversible combination of the toxin and serum components, but to the prevention by the serum of interaction between streptolysin S and erythrocytes.

In addition, it is also demonstrated that the serum of normal rabbit has a property of preventing the thermal inactivation of streptolysin S.